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January 4, 2012

Caryn Cohen, M.S.
Office of Science
Center for Tobacco Products
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

Re: Docket No. FDA-2011-N-0002

Dear Ms. Cohen:

R. J. Reynolds Tobacco Company ("RJRT") hereby submits these documents for consideration in support of the work of the Tobacco Products Scientific Advisory Committee ("TPSAC") during review of the impact of dissolvable tobacco use on public health. Section 907(f) of the Food, Drug, and Cosmetic Act ("FDCA"), as amended by The Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act" or "the Act"), requires the Food and Drug Administration ("FDA") to refer the issue of "the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children" to the TPSAC, which must then provide a report and recommendation to FDA.

During the July 21, 2011 TPSAC meeting on dissolvable tobacco products, RJRT was provided an opportunity to address the TPSAC on the nature and impact of the use of dissolvable tobacco products on the public health, including population-level effects that may be associated with an increased prevalence of use of dissolvable tobacco products. As noted during the presentation, the availability of epidemiological studies examining the comparative health risks and tobacco use patterns associated with dissolvable tobacco products is limited. However, considerable data are available for the tobacco product category, *i.e.*, low-nitrosamine smokeless tobacco ("LN-SLT") products. Therefore, in addition to findings specific to dissolvable tobacco products, RJRT provided a comprehensive summary of the available data on: (1) the potential for dual use of cigarettes and smokeless tobacco to increase toxicant exposure, and hence the risk for disease; (2) the potential for dual use to impede smoking cessation; and, (3) the potential for smokeless tobacco use to increase cigarette smoking (*i.e.*, gateway effect). RJRT noted the following key points:

- A number of public health organizations have acknowledged that the risk for disease associated with LN-SLT use is significantly lower than that associated with cigarette smoking. An expert panel of tobacco researchers from the United

States estimates the excess relative risk for LN-SLT use to be 10% or less of that associated with smoking.[1]

- Studies conducted in Sweden consistently show that use of snus — a type of LN-SLT — is more likely to reduce toxicant exposure (and disease risk), more likely to increase smoking cessation, and more likely to serve as a gateway away from (instead of towards) cigarette smoking.

While available studies conducted in the United States would appear to support an overall population-level benefit associated with increased smokeless tobacco use compared to cigarette smoking, the actual population data needed by FDA and TPSAC to make informed decisions regarding the use of dissolvable tobacco products are unlikely to be available in the near term. In the absence of sufficient population data, models can be used to estimate the effects of different tobacco exposure patterns on population mortality.

During the July 21, 2011 TPSAC meeting, RJRT introduced and provided findings from a dynamic population model developed under contract between RJRT and ENVIRON as a shared resource for public health researchers and policymakers to help clarify assumptions underlying the arguments for and against policies being considered. This model estimates all-cause mortality for a hypothetical population of never tobacco users who, as they age, may transition between different tobacco exposure states, *i.e.*, up to 33 possible transitions into and out of tobacco use. RJRT believes that — absent a robust data set of actual population data — this model may be particularly informative and useful during the TPSAC's review of the potential population-level effects associated with dissolvable tobacco use and as FDA examines and develops tobacco harm reduction policies. The model allows for a direct comparison of different exposure scenarios while holding constant other assumptions underlying the arguments for policies being considered.

RJRT hereby submits the following documents with the intent of providing additional information on the dynamic population model discussed above: (1) a summary document of model input (Attachment 1); and, (2) recent presentations of the model (Attachments 2-6). Draft manuscripts that provide information on the technical aspects of the model, including the model's validation, and summarize early hypothesis testing (e.g. sensitivity analysis) will be provided for TPSAC consideration following acceptance for peer-reviewed publication.

Respectfully submitted,

James E. Swauger, Ph.D., DABT
Vice President – Regulatory Oversight
R. J. Reynolds Tobacco Company

[1] Levy, D.T., Mumford, E.A., Cummings, K.M., Gilpin, E.A., Giovino, G., Hyland, A., Sweanor, D., Warner, K.E. (2004). The Relative Risks of a Low-Nitrosamine Smokeless Tobacco Product Compared with Smoking Cigarettes: Estimates of a Panel of Experts. Cancer Epidemiol Biomarkers Prev 13(12); 2035-42.

Attachments:

Attachment 1 - model input summary, entitled "DATA AND DATA SOURCES FOR . . ."

Attachment 2 - Tobacco Merchants Association Conference oral presentation (2008), entitled "Evidence-based decision making and tobacco harm reduction modeling: opportunities and barriers" (Sulsky)

Attachment 3 - American College of Epidemiology poster presentation (2010), entitled "Development of a dynamic simulation model to estimate population mortality effects resulting from the availability of smokeless tobacco products" (Bachand et al.)

Attachment 4 - American College of Epidemiology poster presentation (2010), entitled "Assessment and application of the multistate life tables approach to modeling population harm reduction with smokeless tobacco" (Sulsky et al.)

Attachment 5 - Congress of Epidemiology poster presentation (2011), entitled "Changes in tobacco-related mortality due to reduced exposure products: a dynamic population model to estimate the potential efficacy of tobacco harm reduction approaches" (Bachand & Sulsky)

Attachment 6 - description and use of model in critique of "Quantifying the effects of promoting smokeless tobacco as a harm reduction strategy in the USA" by Mejia AB, Ling PM, Glantz SA. Tobacco Control 2010 (Bachand & Sulsky)